Window into the Heart

Benico Barzilai, M.D.
Cardiology
Little more than a year ago, a mummified child from the Saint Louis Science Center was brought to Washington University Medical Center as part of a research study that included computed tomography scanning, DNA testing, and radiocarbon dating. When study results were announced at the March 15th Science Center news conference, media around the world—including ABC’s Good Morning America, the Washington Post, and China’s Xinhua News Agency—were fascinated with the story of this unknown child. Scientific findings showed that the mummy was a male infant (age: six to eight months) and lived approximately 2,000 years ago.

For more information about the child mummy exhibit at the Science Center, visit www.slsc.org. For more information about the Institute’s involvement in this research, visit the Electronic Radiology Lab at http://erl.wustl.edu/

Photograph by Kimberly Kania, MIR Photography Lab.
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Matching Program results are in

The 2007-2008 resident training programs begin on July 1. This year, the Institute welcomes 18 trainees who come from these excellent schools:

- David Geffen School of Medicine at the University of California, Los Angeles
- University of Alabama School of Medicine
- Vanderbilt University School of Medicine
- University of Wisconsin School of Medicine and Public Health
- University of Iowa Roy J. and Lucille A. Carver College of Medicine
- Emory University School of Medicine
- Georgetown University School of Medicine
- University of Louisville School of Medicine
- University of Washington School of Medicine
- Indiana University School of Medicine
- Southern Illinois University School of Medicine
- Saint Louis University School of Medicine
- University of Utah School of Medicine
- The Chicago Medical School at Rosalind Franklin University of Medicine and Science
- Washington University in St. Louis School of Medicine

39th Wilson Award presented

Jennifer (Jeni) Sprague, a student in the Medical Scientist Training Program, received the 2006-2007 Hugh M. Wilson Award for Meritorious Work in Radiology. The award honors Mallinckrodt Institute’s second director and is presented as part of Washington University in St. Louis School of Medicine’s (WUSM’s) commencement program.

Sprague earned an undergraduate degree in biochemistry (with highest honors) at Indiana University and received a combined medical/doctoral degree at WUSM. She completed her doctoral research in Mallinckrodt Institute’s Radiological Chemistry Laboratory.

Under the mentorship of Carolyn Anderson, PhD, professor of radiology and associate professor of molecular biology and pharmacology, Sprague’s research combined basic science and translational research in the evaluation of radiopharmaceuticals for early diagnosis and monitoring of cancer metastasis using positron emission tomography (PET).

As a result of Sprague’s work involving the radiochemistry, characterization, and biological evaluation of copper-64, a tracer used with PET for cancer imaging, her research was published in four scientific journals: Clinical Cancer Research, Nuclear Medicine and Biology, Journal of Nuclear Medicine, and the Journal of Medicinal Chemistry.

“While performing her dissertation research in my lab, Jeni had outstanding ideas toward the progress and direction of her project and demonstrated scientific maturity well beyond her age and experience,” says Anderson. “Jeni’s insight and curiosity have led to some very exciting discoveries regarding the development of novel imaging agents and imaging strategies. What makes her truly exceptional, however, is the combination of her scientific and personal maturity, profound curiosity, and unbelievable organizational and time-management skills. I have been extremely fortunate to have a student of such caliber working in my group.”

Welch speaks at Nobel Conference

Michael Welch, PhD, professor of radiology, of chemistry, and of molecular biology and pharmacology, presented an overview of “PET imaging using nonstandard radionuclides” at the Nobel Conference, Watching Life through Molecular Imaging. The conference was held in the Nobel Forum—where the Nobel Prize in Physiology or Medicine is selected—at the Karolinska Institute in Stockholm, Sweden. Prior to the Nobel Forum, Welch, cochief of Mallinckrodt Institute’s Division of Radiological Sciences, was keynote speaker at the 17th International Symposium on Radiopharmaceutical Sciences in Aachen, Germany.
MIR team excels in imaging interpretation

The Institute’s diagnostic radiology resident/faculty team was the big winner—for the third time—in the Philips Vydareny Imaging Interpretation Competition at the 55th Annual Meeting of the Association of University Radiologists (AUR). Team members: doctors Kristopher Cummings, Joseph Erinjeri, and Jack Jennings—2006-2007 diagnostic radiology chief residents; Constantine Raptis—second-year resident; Jennifer Demertzis, Meghan Lubner, and Sara Rohr—third-year residents and the 2007-2008 diagnostic radiology chief resident; Jeffrey Carenza—fourth-year resident; Daniel Wessell, musculoskeletal radiology clinical fellow and 2005-2006 diagnostic radiology chief resident; Jennifer Gould, assistant professor of radiology and director of the Diagnostic Radiology Residency Training Program at Mallinckrodt Institute; Christine Menias, assistant professor of radiology and residency program assistant director; and Sanjeev Bhalla, assistant professor of radiology and residency program assistant director.

Research fellowship is available

Bayer HealthCare has funded a fellowship for research involving contrast-enhanced magnetic resonance imaging (MRI). Jeffrey Brown, MD, professor of radiology, director of clinical research, and cochief of body MRI, will administer the one-year fellowship that will begin in November 2007. For more information about the fellowship and the application process, go to the Mallinckrodt Institute of Radiology Web site at www.mir.wustl.edu.

WUSM among nation’s top schools

In the 2007 U.S. News & World Report rankings, Washington University in St. Louis School of Medicine (WUSM) retained its fourth overall ranking among research-oriented medical schools and continues to hold first place in student selectivity (based on college grade-point averages and MCAT scores). Among the top schools are Harvard University (ranked first); Johns Hopkins University (second); University of Pennsylvania (third); University of California, San Francisco (fifth); University of Washington (sixth); Stanford University (seventh); Duke University and Yale University (tied for eighth place).
Inside the procedure room, the patient's computed tomography (CT) scan shows a tiny tumor sitting squarely in the middle of his left kidney—a challenging spot for resection. Further complicating this case is the patient’s medical history. Years before, he had lost his right kidney to another tumor, and removing too much of his remaining kidney will compromise its function, sentencing him to a lifetime of dialysis treatment.

For most patients with early-stage kidney tumors, surgery is still the standard of care. But this man, like a growing number of others for whom surgery is not an option, will undergo a newer, less-invasive radiological procedure: cryoablation. On the CT image, the two percutaneously (through the skin) placed needles appear, releasing a liquefied, inert gas (argon) into the tumor area. Suddenly, an ice ball forms, enveloping the tumor. After 10 minutes of freezing, five minutes of thawing with helium gas, and 10 more minutes of freezing, the procedure is complete.
Weeks later, during the patient’s follow-up examination, the tumor appeared to be totally destroyed, says Daniel Brown, MD, an interventional radiologist at Mallinckrodt Institute who performed the cryoablation in collaboration with urologic surgeon Sam Bhayani, MD. The two physicians have collaborated on the 25 cryoablations that have taken place at Barnes-Jewish Hospital over the past two years.

Before each procedure, the patient is seen in the Interventional Oncology and Urology Clinic at the Washington University Medical Center so Brown and Bhayani can decide together whether to recommend surgery or cryoablation. After the procedure, the patient is seen in the clinic, and images are reviewed to determine whether the tumor has been adequately treated.

“We have a well-formed cooperative relationship that has let us deliver the best care to the patients,” says Brown, associate professor of radiology and of surgery. “This is an interdisciplinary effort,” adds Bhayani, assistant professor of urology and of surgery. “The patients benefit because they get an opinion from an expert in kidney surgery and from an expert in interventional oncology.”

The procedure Brown and Bhayani have pioneered at Washington University Medical Center, a national leader in ablation, is still considered investigational but has so far had very promising results. Papers published recently by three other medical centers—Johns Hopkins, the Mayo Clinic, and Wayne State University—showed only a handful of recurrences among patients treated by cryoablation during the first year of follow-up care.

“We need to eliminate those recurrences before we can consider this as a replacement therapy for surgery, and we’re still a long way from that. We also need to track its long-term outcome,” says Brown. “But in the meantime, for patients who are not surgery candidates, this is a wonderful option.”

**Background of the Cancer**

Renal cell carcinoma is a fairly rare tumor: seventh or eighth most common among men and twelfth most common among women. In the United States, some 35,000 new cases are diagnosed each year, most of them among people in their 50s. While there is a weak link between smoking and the development of this cancer, the cause is largely unknown. The number of patients with kidney cancer overall is growing, for reasons that are likewise unclear.
Icing Tumors, Saving Lives

We have identified some of the genetics behind renal cell carcinoma,” says Bhayani, “but we don’t know yet why certain genes mutate, causing these cancers to form. So although we’ve made great strides, we don’t have the full information as yet.”

Some 30 years ago, before the advent of CT scans and magnetic resonance imaging, these tumors were nearly always discovered when patients found blood in their urine or felt a pain in their side. By then, the masses were large, up to eight or nine centimeters in size, and surgical removal was the only option.

Bhayani’s study, published in the Journal of Urology in 2006, shows that this picture has changed dramatically. With new imaging technologies, some 80 percent of patients who were recently diagnosed with kidney cancer at Barnes-Jewish Hospital had no symptoms, and their renal tumors were picked up incidentally on CT scans that were taken for other reasons. These masses may be tiny (1 to 4 centimeters in size), which makes them good candidates for ablation.

The Cryoablation Procedure

For years, radiofrequency (RF) ablation—the heat-based cousin of cryoablation—has been used effectively to fight liver, lung, and bone tumors. As in cryoablation, radiologists insert needles into the tumor, but these needles carry a current that heats up the tissue and kills the cells. The problem is that RF ablation is painful and requires significant sedation or general anesthesia. Cryoablation, which is much less painful, works better on kidney cancers and also on patients for whom anesthesia is risky, including those with poor heart function or damaged lungs because of smoking.

Age also is a factor. For older patients, cryoablation may work well, even if its long-term results should prove to be slightly less effective than surgery. “If the cancer comes back in twenty years and the patient is seventy-five or eighty, then the recurrence may not be as emotionally difficult for the patient,” says Bhayani.

Cryoablation—also used by urologists in laparoscopic procedures—involves CT guidance, slender needles, and gases. Once the needles are inserted through the skin and into the kidney, they deliver argon gas into the tumor. The temperature at the needle tip reaches minus 140 degrees, and ice begins forming instantly. Away from the needle tip, the temperature rises somewhat, but a range of minus 20 to minus 40 degrees is still lethal to tumors.

These images taken after cryoablation show an absence of contrast enhancement of the tumor—a finding compatible with a successful procedure.
• Is the ice ball surrounding the tumor? Up to eight needles can be used for a larger area of “cell kill.” “As you put more needles in, it actually becomes a multiplying rather than an additive effect,” says Brown. “The needles synergize, and the ice ball gets bigger.”

The patient stays in the hospital overnight in case of any bleeding complications. With a highly vascular organ like the kidney, there is always the chance of a small vein oozing blood, which could potentially require a blood transfusion.

Pros and Cons of Treatment Options

Surgical excision has a key advantage over cryoablation for small kidney tumors: Surgeons can cut out the mass and send the marginal cells to pathology for analysis, to see whether all the cancer was removed. Since kidney cancer is categorized into five subtypes, each with its own characteristics, cellular analysis also can tell doctors how aggressive the tumor was, which will give them prognostic data.

With cryoablation, radiologists cannot rely on sending a specimen to pathology. Still, the results to date indicate that the procedure is remarkably effective. Preliminary national data shows an effectiveness rate of 93 percent or 94 percent. Of the 25 patients treated at Barnes-Jewish Hospital, only two have had any residual tumor. Both patients were successfully treated at a second visit.

Once kidney cancer has metastasized, it is uniformly fatal, so physicians want to catch any recurrence early on. Radiological follow-up is crucial. After undergoing cryoablation, patients return to Mallinckrodt Institute for CT scans, taken at one month, then three to six months, and thereafter at regular intervals indefinitely. Surgical patients also require follow-up care, though less frequently.

Overall, cryoablation as a treatment for kidney tumors means one more option for patients, say both physicians. “If you are going to offer the full range of treatments for patients with renal cell carcinoma, cryoablation is an important part of their decision making,” says Brown. “Ultimately, patients benefit because they can choose among various options—and all the options are effective,” says Bhayani.

Want more information?

• Kidney Cancer Association: www.kidneycancer.org
• National Cancer Institute: http://cis.nci.nih.gov/
• American Cancer Society: www.cancer.org
Positron emission tomography (PET), an imaging method developed at Mallinckrodt Institute of Radiology (MIR) in the early 1970s, has become a valuable tool in cancer imaging. Malignant tumors tend to devour more sugar (glucose) than do benign tumors. PET imaging of cancer typically involves the use of a radioactive glucose-based analog, or compound, called fluorodeoxyglucose (FDG). Ultimately, abnormal FDG uptake appears as “hot spots” (brighter areas) on PET images. In some types of cancers, it has been shown that if a PET scan is done prior to chemotherapy and again midway through treatment, changes in glucose uptake can be tracked to determine if the tumor is responding to therapy or if the treatment plan should be changed. The patient can then be spared the adverse effects of a therapy that is not affecting the cancer. Now studies have shown that PET is useful in predicting relative survival rates for patients with cervical cancer.
Perry Grigsby, MD, a radiation oncologist and director of the Brachytherapy and microRT treatment centers at the Siteman Cancer Center, says glucose uptake may vary more in cervical cancers than in other types of cancers.

Radiation oncologist Perry Grigsby

Glucose uptake appears to be greater in cervical tumors that are not responding to treatment, independent of the size of the tumor. In Grigsby’s research, each cervical tumor was assigned a maximal standardized uptake value (SUVmax, and referred to in this article as SUV) based on how much glucose was used: the higher the SUV, the higher the risk of lymph node metastases, and the lower the patient’s survival rate.

STUDY FINDINGS

The mean SUV was 10.2 in the first study group of 96 patients. Patients whose tumors had an SUV below the mean had a five-year survival rate of 71 percent; those above, a 52 percent chance of surviving five years without a recurrence.

“By the time an article was published in the April 2006 issue of Gynecological Oncology, we had doubled the number of patients in the study, and it was clear that there were really three demarcations in the data,” says Grigsby, a professor of radiation oncology, of radiology, and of obstetrics and gynecology. “Based on a statistical model, we assigned two hundred and eighty-seven patients into three separate survival-rate groups.”

According to Grigsby, at the patients’ five-year follow-up examinations, the results were remarkable:

- 95 percent of patients with an SUV below 5.2 were disease-free.
- Survival rate for patients with an SUV between 5.2 and 13.3 was 70 percent.
- 44 percent of patients with an SUV over 13.3 were disease-free at five years.

Follow-up examinations at seven to eight years showed more marked differences in the patients who were disease-free:

- 90 percent of patients with an SUV below 5.2,
- 75 percent with an SUV between 5.2 and 13.3,
- 10 percent with an SUV over 13.3.

Grigsby’s research also showed there was a great deal of heterogeneity within the cervical tumors. A tumor’s high SUV score did not apply to the whole tumor, only a part of it. Grigsby and fellow researchers are attempting to identify which areas of the cervical tumor are high in glucose uptake and whether the SUV makes a difference in prognosis.

ADDITIONAL RESEARCH

Another project in the works is examining the genes responsible for high glucose uptake. The research team identified some genetic changes in tumor biopsies; they want to see if those results are consistent across a larger group.

For more information, go to the American Cancer Society Web site: www.cancer.org.
HETEROGENEITY OF FDG UPTAKE IN PRIMARY CERVICAL CANCERS

They also are looking at the role of human papilloma virus (HPV) in those tumors. “We know that ninety-nine percent of cervical cancers are caused by HPV,” says Grigsby. “Once the patient is diagnosed with cancer, physicians typically concentrate on curing the cancer, not the HPV. There’s no consensus as to whether that’s the right decision. When the cancer starts to grow, no one has asked what the current role of HPV is in this disease.”

Grigsby is particularly interested in the virus because of the other HPV-related malignancy—anal cancer. “Both cervical and anal cancers are of the squamous-cell types and are caused by HPV,” he says. “We’ve been using PET to study cervical cancer for nine years, and studies of anal cancer in tandem with cervical cancer have been active for the last two years. The findings are strikingly similar. There’s a good chance that any changes in treatment modalities that come out of this study will apply to both types of cancer.”

PET POTENTIAL

Farrokh Dehdashti, MD, a nuclear medicine physician at MIR, expands on clinical PET studies: “As yet, there are no standards in place for changing a course of treatment based on a tumor’s high FDG uptake, as measured by SUV; thus, we watch these patients closely and use PET following completion of therapy to assess response to therapy and to detect early recurrence.”

Dehdashti, a professor of radiology, is especially encouraged by her research involving the measurement of tumor oxygenation in patients with cervical cancer. “A special hypoxic marker measures the oxygenation of the tumor,” she says. “We know that well oxygenated tumors respond better to radiation as compared to low oxygenated [hypoxic] tumors. Our initial study involved fourteen patients with cervical cancer. Now, we have completed the study of thirty-eight patients and found similar results.”

“The SEER report card [Surveillance Epidemiology and End Results, a source of information on cancer incidence and survival in the United States] published by the National Cancer Institute still ranks cervical cancer as third in the average years of life lost from cancer deaths, ranking behind childhood cancers and testicular cancer, which tends to affect younger, rather than older, men.” —PEBBY GRIGSBY, MD
The PET hypoxic tracer first used by Dehdashti was Copper-60-ATSM (Cu-60-ATSM), which, because it has a 24.5 minute half life, must be produced on a nearby cyclotron. This study was performed with institutional approval and was done at Washington University School of Medicine with the availability of the three cyclotrons housed at Mallinckrodt Institute. In order to make this radiopharmaceutical more widely available, the radiochemistry team wanted to produce Cu-64-ATSM. Since Cu-64 has a 12.7 hour half life, it can be transported to medical centers that are conducting PET studies but do not have an in-house cyclotron.

But first, the research team had to determine if the quality of PET images performed using Cu-64-ATSM was comparable to that of Cu-60-ATSM. In order to study Cu-64-ATSM, it was necessary to obtain an Investigational New Drug (IND) approval from the United States Food and Drug Administration (FDA)—which was obtained with the help of the Development of Clinical Imaging Drugs and Enhancers (DCIDE) program at the National Cancer Institute. Jason Lewis, PhD, an assistant professor of radiology, obtained the toxicology and pharmacology data for Cu-64-ATSM, which was required for approval of the IND by the FDA. Dehdashti and Barry Siegel, MD, a professor of radiology and chief of the Institute’s Division of Nuclear Medicine, have completed a study that compared PET images using both tracers. If there is no clear advantage for using Cu-60, then the Cu-64 tracer can be transported to other study centers, which will greatly expand cervical cancer research.

Editor’s note: Doctors Dehdashti, Ghigsby, Lewis, and Siegel recently were invited to the National Cancer Institute to discuss their role in developing a multicenter trial for Cu-64.

Radiochemist Jason Lewis

The Cu-ATSM hypoxia selective radiopharmaceutical used in the cervical cancer studies at Washington University School of Medicine were developed in Mallinckrodt Institute’s Radiological Chemistry Laboratory as part of the Radionuclide Resource for Cancer Applications, a National Cancer Institute-sponsored program. The following MIR scientists are involved in this program:

- Jason Lewis, PhD, an assistant professor of radiology and codirector of the microPET imaging facility
- Michael Welch, PhD, a professor of radiology and of chemistry and cochief of the Institute’s Division of Radiological Sciences
- Thomas Voller, research laboratory supervisor.
Recent advances in cardiovascular imaging technology promise quicker diagnosis of hidden health threats in some patients. At Washington University in St. Louis, a partnership that combines the top-level expertise of radiologists and cardiologists with the cutting-edge technology of computed tomography (CT) and magnetic resonance imaging (MRI) will provide a greater understanding of coronary artery disease.
This joint venture will create a new imaging group, an interdisciplinary team of radiologists and cardiologists that will be part of Mallinckrodt Institute of Radiology's Cardiothoracic Imaging section. The cardiac imaging staff will be headed by Pamela Woodard, MD, an associate professor at Mallinckrodt Institute, and Benico Barzilai, MD, a professor in the Department of Medicine’s Division of Cardiovascular Disease. The partnership is one of a handful of such interdisciplinary efforts in the country and the only one in Missouri, according to Woodard.

The cardiothoracic imaging group will specialize in cardiac CT angiography, using a CT scanner to produce high-resolution, three-dimensional images of coronary arteries and cardiac anatomy and using MRI to assess cardiac morphology and function. “One exciting aspect of this program is the new CT technology that allows us to acquire volumetric data covering the heart at every phase of the cardiac cycle, very rapidly,” extols Woodard. “The technology gives physicians a noninvasive tool to view cardiac function.”

The speed and resolution of these newest CT scanners has altered the diagnostic landscape. The 64-slice CT scanner takes 64 images (in scanner nomenclature, these are known as slices) in a single revolution around the tube in which the patient lays supine for the exam. The duration that patients must hold their breath during the exam (known as the “breath-hold”) takes only a few seconds. The resulting images are richly detailed, showing the intricacies of the cardiovascular system, including the exterior of coronary arteries and vessels. In contrast, invasive techniques can only reveal what is going on in the interior of the structures.

Cardiac CT angiography is evolving into a powerful tool in the battle against one of the deadliest threats to heart health—coronary artery disease. Sudden cardiac deaths, primarily from heart attack and stroke, number about one-half million in the United States.
To order a cardiac CT or cardiac MRI scan, call Central Scheduling at (314) 362-7111. For same day add-ons or for a physician consultation regarding an examination, page (314) 663-1010. Scheduling of these examinations must be done by a physician or by the physician’s office staff.

Coronary blockages are caused by atherosclerosis, as fatty material collects and thickens along the interior walls of arteries. This hard substance, called plaque, retards blood flow through the artery and also can break off in pieces, causing a heart attack or a stroke. And, blood clots may attach onto plaque material, further restricting blood flow and also presenting the possibility of breaking off and causing a stroke or a heart attack.

Some people experience chest pain as a result of atherosclerosis; tragically for many, there are no symptoms before the disease causes death. For those who do have symptoms, the “gold standard” of screening techniques remains cardiac catheterization. In this procedure, the patient is first injected with a contrast agent. Then the cardiologist inserts a guidewire, and over that a catheter, into a major vein in the groin. As an X-ray views the heart, the physician directs the catheter into the arteries surrounding the heart, using it to introduce additional contrast agent to create more detailed X-ray images.

The advantage of the cardiac catheterization is the ability to combine diagnosis and treatment in one procedure. If the degree of blockage is severe, a different type of catheter can be placed in the vessel and the cardiologist can insert a balloon that is used to destroy the plaque and clots by applying pressure into the balloon and, thereby, against the walls of the artery. Stents and other therapeutic devices can be inserted through the catheter, if needed, to give temporary or permanent support to the artery walls.
Radiologists and cardiologists agree there is a place at the diagnostic table for cardiac CT angiography, but they have yet to decide which patients would most benefit. Because 30 to 40 percent of cardiac catheterizations do not show any blockage, there is great interest in determining a priori whether a particular patient should have the less-invasive CT procedure as an initial screening.

Barzilai acknowledges that many unknowns must be addressed. “On the one hand, there is the question of screening an asymptomatic patient,” he says. “If we find some blockage, there may be some pressure to do something about it, even if it is minor. On the other hand, we aren’t really sure what would happen to that type of patient if they were never evaluated.”

For now, according to Woodard, the test is an excellent alternative for people with atypical chest pain, inconclusive stress tests, and chronic chest pain. Some patients will indeed need to go directly to cardiac catheterization. Others may have noncoronary cardiac disease that the CT option will reveal in great detail, leading to appropriate and targeted treatment.

“Cardiac CT angiography can also help us determine the effect of blockage on blood flow, and that will help us choose the best treatment option,” says Barzilai. “If patients have a less-than-fifty percent blockage, visible on CT, without obstruction of blood flow, then we can treat them with medicine.”

Cardiac MRI also will play a role in this joint venture. A cardiac-gated version of MRI has been available since the late 1980s; however, new developments occur daily. Cardiac MRI, long used for anatomic imaging, is now the reference standard for ventricular function.

“Newer delayed contrast-enhanced techniques can show the exact size and location of myocardial infarction unlike any other test,” says Woodard. “The same technique can be used for characterizing cardiomyopathies not caused by infarction and may provide insight into the etiology of a malfunctioning heart.” Techniques also are available to assess the extent of valve disease and to provide information about whether a heart valve should be replaced.

Both physicians are certain of one thing: The joint venture will lead to better decision making and optimal application of the new technology. They are proud of their role in promoting cooperation between their disciplines. “I hope we will set a benchmark for other institutions,” says Woodard. “Patient care is paramount, not who owns the equipment.”

Barzilai emphasizes the benefits of the approach in teaching young physicians. “I’m excited that I’ll have cardiology fellows sitting next to radiology fellows, treating the same patient. The two disciplines bring different thought processes to the same table. I’ve always believed it’s easier to collaborate with other departments here at Washington University than at other places. I do it on a daily basis. It is one of the strengths of our institution.”

Top: This coronary CT angiogram shows a stenosis (arrow) in the distal right coronary artery (RCA).

Bottom: Delayed contrast-enhanced short axis cardiac MR image demonstrates an inferoseptal subendocardial infarction (arrow) of the left ventricle.
Researchers at Mallinckrodt Institute are hunting for new and effective ways to assess life-threatening risks to adolescents from obesity, and they are forming partnerships with pediatric diabetic specialists and nutrition experts to help these impressionable youngsters lead healthier lives. One key to improving long-term health of overweight teenagers is to understand the location of fat within the abdomen. Magnetic resonance imaging (MRI) turns out to be an excellent tool to map the composition of abdominal fat—external (also called subcutaneous) and internal (or visceral). Visceral fat poses greater danger to internal organs and is associated with diabetes, heart disease, and nonalcoholic fatty liver disease.
Marilyn Siegel, MD, professor of radiology and of pediatrics, is at the forefront of research using imaging techniques to understand abdominal fat distribution. In the March 2007 issue of the journal Radiology, Siegel described her significant work using MRI to assess the distribution of fat in obese preadolescents and adolescents.

MRI had been proven effective for measuring body fat in adults, but only a few studies had been done in children (defined as ages six to 11 years) and adolescents (ages 12 to 19 years). In terms of long-term health and the likelihood of developing serious disease, there is bad fat and there is really bad fat. External fat is easy to see; we even give it names such as “love handles” or “spare tire.” But internal fat, deep inside the body and surrounding abdominal organs, is much harder to assess and much more dangerous to an individual’s health. “Since so many serious illnesses are correlated with intra-abdominal fat, it is critical to find an accurate way to measure it,” says Siegel.

Although causality remains a mystery, the measure of intra-abdominal fat in teenagers is a marker for a future beset by serious complications. The obesity rate among young people is skyrocketing, and pinpointing the presence of visceral fat may help to develop effective prevention through diet and exercise programs that literally get beyond the surface. “We set out to find a fast, reliable, and safe technique to measure fat in children. Different options had been tried in the adult population but not in a pediatric population. We wanted to see if we could improve accuracy and reduce errors that tend to occur in non-radiological evaluations,” says Siegel.

As an Armed Forces Institute of Pathology Distinguished Scientist, Marilyn Siegel, MD, spent six months in Washington, DC, studying the correlation between abnormal radiological images and their underlying pathological processes.

MEASURING BODY FAT

The current standard evaluation to estimate total body fat is anthropometry, a physical examination that measures circumference of the waist and abdomen, height, and body mass index (BMI). Anthropometry, when performed by well-trained practitioners, may yield an accurate measurement of total fat. But the potential for error is high if the practitioners lack training.
Another reliable method for determining total body fat is dual X-ray absorptiometry (DXA). Although DXA is accurate for estimating body fat, this technique requires exposure to ionizing radiation. In addition, both DXA and anthropometry share a disadvantage: Neither test can give a breakdown between subcutaneous fat and the more harmful intra-abdominal fat.

Siegel collaborated with experts at Washington University to measure total and intra-abdominal fat distribution in adolescents. In this study, 30 adolescents had fat tissue measurements taken by single-section and whole abdominal, multi-section MRI. The study’s 20 boys and 10 girls were between the ages of 10 and 18:
- Nine were overweight but did not have diabetes.
- 10 had Type 2 diabetes and were overweight.
- 11 were normal weight and did not have diabetes.

The single-section and multi-section MR measurements were compared and tested for correlations with anthropometric and DXA measurements. The software that made the MR analysis of fat distribution possible was developed in the Electronic Radiology Laboratory at Mallinckrodt Institute. The signal intensity of fat pixels is higher than that of muscle and visceral organ pixels,” explains Siegel. “We can use MRI to separate and to measure images of subcutaneous and visceral fat and to calculate the amount of each type as a percentage of total abdominal area.”

The study produced encouraging results and suggests that MRI can play a leading role in the fight against childhood obesity. Fat measurements using MRI—both single-section and whole-abdominal, multi-section imaging—strongly correlated with anthropometric and DXA calculations. Even better, the single-section examination, which takes just a few seconds, proved to be as accurate as the multi-section examination for characterizing body fat.

**THE MRI STUDY TEAM**

**CLINICAL**
- Marilyn Siegel, MD, professor of radiology and of pediatrics
- Neil White, MD, CDE, professor of pediatrics

**ANALYSIS**
- Kyongtae Bae, MD, PhD, associate professor of radiology
- Charles Hildebolt, DDS, PhD, associate professor of radiology and adjunct associate professor of anthropology
- Cheng Hong, PhD, MD, research associate
While all study volunteers had similar fat distribution patterns with a predominance of fat in the tissues of the abdominal wall, the total amount of fat varied. Overall fat volume was highest in the diabetic, overweight adolescents.

“Now we have a safe, accurate, and fast screening tool. Speed is an important factor when working with young patients,” says Siegel. “It’s difficult to keep them immobile for a lengthy examination.”

**FORGING PARTNERSHIPS**

Washington University’s leadership in the study and treatment of obesity-related illness is leading to some exciting partnerships between radiologists and internists. Mallinckrodt Institute researchers are contributing creative thinking about the applicability of MRI and ultrasound; University investigators and clinicians bring knowledge and sensitivity to patients (especially younger ones) as well as the nuances of treating a disease with a large behavioral component.

In a separate study involving adolescent obesity, Siegel is collaborating with other Washington University researchers to determine if ultrasound—an inexpensive, readily available, noninvasive technology—is a viable tool for diagnosing non-alcoholic fatty liver disease (NAFLD). Little is understood about the cause of NAFLD, but most specialists agree that it is closely linked to increasing rates of obesity.

“There is great concern about the increasing prevalence of NAFLD in children,” says Siegel. “NAFLD has been reported to affect twenty-three percent of overweight children. Yet they may be completely asymptomatic until the liver is severely damaged.”

Not all cases of NAFLD result in symptoms or other problems, and the course of the disease is being investigated in both adults and children. Until now, the recommended test for detecting NAFLD has been proton magnetic resonance spectroscopy, an expensive technique requiring specialized equipment and expertise.

Siegel reports that in her study of 28 overweight adolescents, ultrasound was a reliable tool for diagnosing moderate to severe NAFLD. However, she concludes that additional studies to detect mild NAFLD are needed.
Siegel and the research team are passionate about making a difference in young people’s lives. “If we successfully monitor the progress and effectiveness of different strategies, we can keep children and teenagers from becoming patients in the liver transplant program and in the cardiac catheterization and renal dialysis labs. It’s important to help them make the connection between being overweight and developing a life-threatening disease,” observes Siegel.

“Their mantra has become, ‘I’m too young for that; I won’t get sick.’ But in St. Louis, in Missouri, in the United States, young people are becoming very ill as their health falls prey to obesity,” she adds. “We need to help these kids, and their parents, to recognize the dangers and to help them take action. The MRI procedures we have developed are potentially useful in many clinical and research applications, including planning patient management, monitoring therapeutic interventions, and implementing multicenter clinical trials.”

**AMERICAN YOUTH AT RISK**

**OVERWEIGHT VS. OBESE**
- Overweight children (defined as ages 6 to 11 years) and adolescents (ages 12 to 19 years) are defined as being at or above the 85th percentile of Body Mass Index (BMI); obese children and adolescents, at or above the 95th percentile.
- Some researchers refer to the 95th percentile as overweight, while others refer to it as obese. The Centers for Disease Control and Prevention (CDC), which provides national statistical data for the weight status of American youth, avoids using the word “obesity” and identifies every child and adolescent above the 85th percentile as “overweight.”

**UNITED STATES STATISTICS**
- The percentage of young people who are overweight has more than tripled since 1980.
- Approximately 30.3 percent of children are overweight, and 15.3 percent are obese. For adolescents, 30.4 percent are overweight and 15.5 percent are obese.
- Sixteen percent (nine million) of children and adolescents are overweight.
- Four in 10 Mexican-American and African-American children and adolescents are overweight or are at risk of being overweight.
- About sixty percent of obese children ages 5 to 10 years have at least one cardiovascular disease risk factor, including high cholesterol and triglycerides, increased insulin levels, or high blood pressure. One fourth of these children have two or more risk factors.
- Children and adolescents who are overweight by the age of 8 years are 80 percent more likely to become overweight or obese adults.
- Obesity is the second leading cause of all preventable deaths in the United States.

Information available on these Web sites.
Shape of the Nation Report 2006: www.aahperd.org/naspe/ShapeOfTheNation/PDF/ShapeOfTheNation.pdf
Keeping Tabs on

Multiple Sclerosis

Researchers are using magnetic resonance imaging to study myelin and nerve damage

by Mary Jo Blackwood, RN, MPH

Multiple sclerosis (MS) is a devastating, and as yet, incurable autoimmune disease that affects the central nervous system. According to the National Multiple Sclerosis Society (NMSS), anyone can develop MS; however, the typical candidate is between the ages of 20 and 50, a woman (two to three times more often than a man), and of Northern European descent. About 400,000 Americans acknowledge having MS. Worldwide, that number may be 2.5 million.

The exact cause of MS is unknown but, according to researchers, symptoms of MS probably are caused by damage to the myelin sheath protecting nerves and/or by damage to the nerves themselves. Tracking that damage is becoming easier because of new imaging techniques that can help to predict outcome and prognosis, as well as to differentiate between MS and other clinical, less severe look-alikes.

The NMSS is currently funding three studies at Mallinckrodt Institute of Radiology that involve diffusion tensor imaging (DTI), a magnetic resonance imaging (MRI) technique that enables the measurement of the restricted diffusion of water in tissue. DTI's principal application is in the imaging of white matter where the location, orientation, and direction of water molecule movement can be measured.

Here, the lead investigators discuss their important research.
Sheng-Kwei (Victor) Song, PhD

Song, an associate professor of radiology in the Biomedical Magnetic Resonance Laboratory, has a three-year NMSS grant to study the use of DTI in differentiating between damage to myelin and damage to the nerve fibers in people with MS.

"Based on our work using animal models of MS and other white matter disease and injury, we found that the movement of water molecules in nerve fibers is a potential marker for nerve injury," says Song. "Our research team was able to conduct DTI studies on nerve fibers from mouse models of MS in vivo and confirm our findings through histological analyses."

"The current findings suggest that this method is capable of noninvasively reflecting damages to nerve fibers and the protective myelin sheath in the animal model," he adds. "We want to see if these results with animal models can translate to patients with optic neuritis, an early sign of MS."

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Song is working with groups of patients with optic neuritis (an early sign of MS that results in temporary or permanent vision loss) to determine if DTI measurements are predictive of good and bad recovery. In the first study, the correlation of DTI results indicating nerve injury will be compared to visual function in patients with chronic optic neuritis. Since myelin can regenerate and nerves cannot, Song is studying both patient groups, hoping to make a correlation between nerve damage, myelin damage, or both.

The next study will examine patients at the onset of optic neuritis, and then again at three, six, and 12 months afterwards to track changes and to determine if poor outcomes can be predicted. During active optic neuritis, patients with and without nerve or myelin damage will have similar symptoms; DTI may give the treating physician the currently unavailable information on prognosis and treatment stratification. Song also is looking at spinal cord damage in patients with MS.

"It was reported that ninety percent of patients with MS have spinal cord lesions over the duration of the disease," says Song. "In a recent study of mouse models of MS, our spinal cord DTI analysis not only identified the diseased animals from the control but also correctly differentiated the diseased animals with different degrees of disabilities. We believe that our method will be able to predict the severity of disability resulting from the spinal cord lesions in patients with MS."
Joshua Shimony, MD, PhD

"A wonderful property of MRI is that the signal can be conditioned to produce different types of images," says Shimony, an assistant professor of radiology and a neuroradiologist. "With DTI, the signal can be programmed for sensitivity to microscopic movement of water molecules. Diffusion motion is determined by a number of factors. Take a bucket of water and drop a dot of ink into it, and the ink spreads evenly in all directions. That's an example of unrestricted diffusion."

"In the brain or other biologic tissue, there are many restrictions to water movement: proteins, cell walls, blood vessels, and the like," he adds. "All of these will block water from spreading uniformly."

"Much can be learned from the study of MS with DTI, since myelin is a major cause of restriction in the brain," says Shimony. "Myelin forms the insulator around nerve fibers and restricts water flow in a certain way. As myelin is destroyed, the diffusion patterns change, and we can see less restriction."

Shimony keeps up with Song's research and looks at different aspects of the same problem in his NMSS pilot grant to study brain tissue by using a variation of DTI.

"Hundreds of scientific papers have been written about the results from using the DTI model. But, in the lab, we have found some limitations, and there have been some variations proposed to describe the biology better. My proposal to the MS Society is to study a new model (which we called the constant-offset version of DTI, or DTCO), involving patients with mild and severe MS as well as patients with no disease (called controls), to determine whether this model is more useful for staging the diagnosis. Constant offset was the simplest way to change the model and has been shown by others in our lab to fit the data better," he says.

DTCO detects water molecules that are highly restricted in their motion, such as those near a cell boundary. Early findings indicate this technique may increase the ability of DTI to detect differences in types of tissue damage. Shimony, with the assistance of Larry Brethorst, PhD, a staff scientist in the Institute's Biomedical Magnetic Resonance Laboratory, developed the software to analyze data with the new model, and 12 patients have already been scanned by Shimony's research assistant Adrian Epstein. After 15 patients (the study's goal) have been scanned, Shimony will analyze the data and compare it to the data from control subjects that have been scanned previously. Hopefully, the constant-offset model will provide new noninvasive ways to view different types and amounts of tissue damage and tissue recovery; all are important in predicting prognosis and the effect of different therapies on the disease.

"The information gains should help to target additional research that will further the quest for a cure," says Shimony.
Patients with MS can have **one of four forms** of the disease. Each form of MS can produce **mild, moderate, or severe symptoms**.

**Relapsing-Remitting**—Most common (85%). Patients experience flare-ups (also called relapses, attacks, or exacerbations). Includes episodes of acute worsening of neurological function, followed by partial or complete recovery (remission).

**Primary-Progressive**—Rare (approximately 10%). Patients experience slow but continuous worsening of the disease from the onset, with no distinct relapses or remissions. Includes variations in rates of progression over time, occasional plateaus, and temporary minor improvements.

**Secondary-Progressive**—Before the availability of “disease-modifying” drugs, one half of patients with relapsing-remitting MS developed the secondary-progressive form of the disease within 10 years of their initial diagnosis. Patients experience an initial period of relapsing-remitting MS, followed by steadily worsening symptoms (with or without occasional flare-ups), minor recoveries (remissions), or plateaus. Long-term data are not yet available to demonstrate if development is significantly delayed by treatment.

**Progressive-Relapsing**—Rare (approximately 5%). Patients experience steadily worsening symptoms from the onset but also have clear, acute relapses (attacks or exacerbations), with or without recovery. The periods between relapses are characterized by continuing disease progression.

Additional information available on the National Multiple Sclerosis Society Web site: www.nationalmssociety.org.

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Tammie Benzinger, MD, PhD

Benzinger, an instructor in radiology and a neuroradiologist, has an NMSS pilot grant to study perhaps the most vulnerable segment of the MS population: children. Although MS is largely an adult disease, 2.5 percent of MS patients are children—and their prognosis is usually more serious. Children also are more prone to other diseases such as acute disseminated encephalomyelitis (ADEM), which can be an MS look-alike.

“ADEM can occur after a viral or bacterial infection, or even after an immunization. It is a self-limiting autoimmune response in the brain. In children who have ADEM, symptoms usually regress within three months, even without treatment,” explains Benzinger. “However, those symptoms can mimic a chronic debilitating disease like MS, which should be treated early. A certain number of children with ADEM do recover but develop MS in adulthood. The problem is how to determine injury to the nerves versus the reversible myelin injury. If patients have nerve injury, even if the symptoms go away, they seem to be at greater risk for MS later.”

“This study is a clinical application of Doctor Song’s work with the mouse model,” she adds. “My hypothesis is that the nature of the white matter lesions can be discriminated between myelin injury and axon injury in human patients by using DTI as the MR biomarker for white matter injury.”
The histopathology of ADEM and pediatric MS are markedly similar: Both have demyelination, inflammation, and axon injury, but in different proportions. Even in fatal cases, ADEM demyelination has limited axon loss (nerve injury). However, in patients with MS, axon loss occurs early in the disease—most prominently within the first year—so early treatment is crucial. Benzinger believes that by using DTI, physicians could differentiate between myelin and nerve injury, giving a better indication as to whether the patient should be closely monitored or started on aggressive therapy. Current guidelines for MS stress early treatment for the best outcomes.

Her study involves ill children during the acute phase of ADEM. Up to 20 percent of patients initially diagnosed as having ADEM are later reclassified as having MS. “There are no large studies of these children,” Benzinger says. “I’m collaborating with Doctor Soe Mar, from the pediatric neurology department at Saint Louis Children’s Hospital, who runs a clinic for pediatric demyelination. By comparing the disease process of children diagnosed with ADEM or MS and of children who are experiencing a first demyelinating event, we hope to determine whether DTI results can be useful to diagnose or to confirm suspected diagnoses in these children.”

Early, accurate differential diagnosis of these diseases could be critical to children and to their families by quickly identifying children who could benefit from early treatment of MS and sparing those with ADEM whose symptoms will regress without treatment.  

“The problem is how to determine injury to the nerves versus the reversible myelin injury...”
RESEARCH STUDY

• WOULD YOU LIKE TO HELP RESEARCHERS LEARN MORE ABOUT MEMORY CAPABILITY IN OLDER ADULTS?

• DO YOU HAVE A BROTHER OR SISTER WHO IS WITHIN FOUR YEARS OF YOUR AGE?

• ARE YOU OR YOUR SIBLING BETWEEN THE AGES OF 70 AND 75?

Volunteers are needed for a Washington University School of Medicine/Mallinckrodt Institute of Radiology brain imaging study. Both you and your sibling must be able to participate in the study. Note: if you have had a metal device, such as a pacemaker, implanted due to surgery or injury, you may not be eligible for the study.

Eligible volunteers will undergo the following:
• positron emission tomography (PET) scan
• magnetic resonance (MR) scan
• memory assessment

Volunteers will be compensated for their time and participation.

FOR MORE INFORMATION, CALL 314-362-1558.
In this section, the names of employees who are full-time faculty or staff or who have an appointment in the Department of Radiology are highlighted in boldface type.

**NEW FACULTY**

William Spees, PhD, research instructor in radiology, Division of Radiological Sciences.

**JOINT APPOINTMENTS**

Dione Farria, MD, MPH, assistant professor of radiology, was appointed adjunct professor, Department of Community Health, Saint Louis University School of Public Health.

**GRANTS**

Tammie Benzinger, MD, PhD, instructor in radiology, as principle investigator, received a $44,000 pilot grant from the Multiple Sclerosis Society for her research on “Directional diffusivity as an MR biomarker in childhood demyelinating disease.” Coinvestigators for the one-year grant are Soe Mar, MD, Department of Neurology; Sheng-Kwei Song, PhD, associate professor of radiology; and Anne Cross, MD, Department of Neurology.

Delphine Chen, MD, instructor of radiology, as principal investigator, received a $772,355 grant from the National Institutes of Health/National Institute of Biomedical Imaging and Bioengineering to study “Apoptosis and inflammation imaging.” Mentors for the five-year grant are Robert Mach, PhD, professor of radiology and of cell biology and physiology; and Mark Mintun, MD, professor of radiology and of psychiatry. She also received a $460,000 grant from the Damon Runyon Cancer Research Foundation to investigate “Apoptosis imaging.” Mentors for the three-year Clinical Investigator Award are Mach and Michael Welch, PhD, professor of radiology, of chemistry, and of molecular biology and pharmacology.

Nirvikar Dahiya, MD, abdominal imaging clinical fellow, as principal investigator, received a $10,000 Education and Research grant from the American Institute of Ultrasound in Medicine to study “Tendinopathy of the rotator cuff: correlation of ultrasonographic findings with histopathologic changes using a cadaver shoulder model.”

Igor Efimov, PhD, associate professor of biomedical engineering and of radiology, received a four-year subcontract in the amount of $805,819 from the National Institutes of Health to investigate “Defibrillation mechanisms in infarcted hearts.” As principal investigator, he received a two-year, $143,000 grant-in-aid from the American Heart Association for research on “Structure of the human AV junction.”

Dione Farria, MD, MPH, assistant professor of radiology, received a $10,350 STEP grant from the St. Louis Affiliate of Susan G. Komen for the Cure to study “Reducing delays in breast cancer diagnosis in the St. Louis Public Safety Net system.” Coinvestigators are Katherine Matthews, MD, Department of Obstetrics and Gynecology; and Susan Kraenzle, RN, manager of the Breast Health Center at the Alvin J. Siteman Cancer Center.

Jeffrey Lin, MD, PhD, a third-year diagnostic radiology resident, received a $30,000 seed grant from the Radiological Society of North America to study “Noninvasive characterization of NFkB activation in non-alcoholic fatty liver disease.”

David Piwnica-Worms, MD, PhD, professor of radiology and of molecular biology and pharmacology, is faculty mentor for the one-year grant.

Joel Perlmutter, MD, professor of neurology, of radiology, and of physical therapy, received a National Institutes of Health subcontract of $195,000 to investigate “Pathophysiology of dystonia and parkinsonism.” The subcontract is through a five-year grant awarded to Jonathan Mink, MD, University of Rochester. As principal investigator, Perlmutter received a one-year, $50,000 grant from the Huntington Disease Society of America for his project “Huntington’s Disease Center of Excellence.”

Joshua Shimony, MD, PhD, assistant professor of radiology, received a $125,000 grant from the National Institutes of Health/National Institute of Child Health and Human Development for research on “A Bayesian approach to MRT tractography in the developing brain.” Coinvestigators for the five-year grant are Jeffrey Neil, MD, PhD, professor of neurology, of pediatrics, of neurological surgery, and of radiology; Terrie Inder, MD, Department of Pediatrics; Robert McKinstry, MD, PhD, associate professor of radiology; and Larry Brethorst, PhD, staff scientist.

Marilyn Siegel, MD, professor of radiology and of pediatrics, received a $30,000 seed grant from the Radiological Society of North America for research on “Hyperpolarized helium-3 MRI assessment of bronchiolitis obliterans in pediatric lung transplant recipients.” Collaborators for the one-year grant are Dmitriy Yablonskly, PhD, professor of radiology and of physics; Mark Conradi, PhD, professor of physics, of radiology, and of chemistry;

David Gierada, MD, PhD, associate professor of radiology and anatomy; and Stuart Sweet, MD, PhD, Department of Pediatrics.
Karen Wooley, PhD, professor of chemistry and of radiology, was appointed to the editorial advisory boards of Bioconjugate Chemistry and the Journal of the American Chemical Society. She was appointed to the External Advisory Committee of the National Science Foundation-Partnership for Research and Education in Materials (NSF-PREM) Program with the University of California, Santa Barbara. She also was appointed chair of the 2007 Polymers (East) Gordon Research Conference.

Karen Wooley, PhD, professor of chemistry and of radiology, received a two-year grant of $200,000 (total award) from Children’s Discovery Institute, a research partnership between St. Louis Children’s Hospital and Washington University in St. Louis, for research on “Hyperbranched fluoropolymers (HBFP(III)), designed as complex nanostructures for imaging and therapeutic delivery in the diagnosis and treatment of pediatric brain cancers.”

Yasha Kadkhodayan, MD, first-year diagnostic radiology resident, received a 2007 Society of Interventional Radiology Resident-in-Training Scholarship, which funded his attendance at the Society’s 32nd Annual Scientific Meeting in Seattle, Washington, March 1-6.

Jonathan McConathy, MD, PhD, a second-year diagnostic radiology resident, was one of 80 residents nationwide chosen to participate in the Introduction to Research Program at the American Roentgen Ray Society’s 107th Annual Meeting in Orlando, Florida, May 6-11.

Constantine Rapitis, MD, a second-year diagnostic radiology resident, was one of 35 residents in the United States selected to attend the Siemens—Association of University Radiologists (AUR) Radiology Resident Academic Development (SARRAD) Program at the AUR’s 55th Annual Meeting in Denver, Colorado, April 24-28.

Igor Efimov, PhD, associate professor of biomedical engineering and of radiology, presented “New approaches to device therapy of cardiac arrhythmias: insights from optical imaging” at the Bioengineering Leaders Seminar Series, sponsored by the Department of Biomedical Engineering, Duke University, Durham, North Carolina, January 8. He presented “Optical imaging of arrhythmias” at the University of Missouri—St. Louis, January 12. He spoke on “New advances towards painless defibrillation” and “Sinoatrial and atrioventricular nodal function and structure” at the University of California, Santa Barbara. She also was appointed chair of the 2007 Polymers (East) Gordon Research Conference.

Yoram Rudy, PhD, professor of engineering, cell biology and physiology, and of medicine, and research professor of radiology, was elected to a one-year term on the Board of Directors for the International Society for Computerized Electrocardiology. He was elected to a two-year term as president of the Cardiac Electrophysiology Society.

Dionne Farria, MD, MPH, assistant professor of radiology, spoke on “Imaging approach to the symptomatic breast” and “Imaging evaluation of breast implants” at Women’s Health and Imaging in a Digital Environment, San Antonio, Texas, January 22. She presented “Screening strategies and minority outreach” at the Cancer Centers Administrators Forum Annual Meeting, St. Louis, Missouri, March 26.


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Jay Heiken, MD, professor of radiology, as visiting professor, spoke on “CT of the abdominal aorta: diagnosing aneurysm rupture” and “Distinguishing benign from malignant liver lesions with CT and MRI” at the Medical College of Wisconsin, Milwaukee, January 22. He presented “CT colonography for colorectal cancer screening: current status”; “Benign liver masses: detection and characterization with CT and MRI,” and “Hepatocellular carcinoma: imaging evaluation with MRI” at Cancer Imaging 2007, the Joint Meeting of the International Cancer Imaging Society and the Hong Kong College of Radiologists, Hong Kong SAR, People's Republic of China, February 10 and 11.

Jason Lewis, PhD, assistant professor of radiology, spoke on “PET imaging of cancer with copper-64-thiosemicarbazones” at the Joint Program in Nuclear Medicine, Harvard Medical School, Boston, Massachusetts, January 18.

Robert McKinstry, MD, PhD, associate professor of radiology, spoke on “The triple threat: living the dream” at the Harvard-Massachusetts Institute of Technology Division of Health Sciences and Technology Alumni Roundtable, Boston, Massachusetts, May 1.

Yoram Rudy, PhD, professor of engineering, cell biology and physiology, and of medicine, and research professor of radiology, presented “From genetics to cellular function using computational biology” to the Center for Neurodynamics, Department of Physics and Astronomy, University of Missouri—St. Louis, February 23. He spoke on “Computational biology and noninvasive imaging of cardiac arrhythmia” at the Frontiers in Human Pathobiology Seminar Series, Washington University in St. Louis School of Medicine, St. Louis, Missouri, March 7. He spoke on “Cardiac Repolarization and Arrhythmia: mechanistic insights from computational biology” at the Cardiovascular Research Center, Department of Medicine, University of Iowa, Iowa City, March 9. He presented “Imaging Arrhythmias in humans: electrocardiographic imaging (ECGI)” at the Gordon Research Conference on Cardiac Arrhythmia Mechanisms, Ventura Beach, California, March 18.

Barry Siegel, MD, professor of radiology and of medicine, spoke on “National Oncologic PET Registry (NOPR),” “PET/CT of gynecologic cancers,” and “PET/CT of breast cancer” at the First Annual PET/CT Update, sponsored by the American College of Radiology, Boca Raton, Florida, January 28-31. He presented “PET/CT in oncology diagnosis”; “Evolution of PET reimbursement and the National Oncologic PET Registry”; and “PET in oncology: beyond FDG” at the 22nd Annual Cross-sectional Imaging Conference, sponsored by the University of Pennsylvania School of Medicine, St. John, U.S. Virgin Islands, February 26-March 2. He spoke on “National Oncologic PET Registry,” “Update: PET/CT in lung cancer,” and “Update: PET/CT in gynecologic malignancies” at Updates on PET/CT Imaging for Referring Physicians, sponsored by Mount Sinai School of Medicine, New York, New York, April 20.

Biello Lecture

David Townsend, PhD, director of the Cancer Imaging and Tracer Development Research Program, University of Tennessee Medical Center, was guest lecturer for the 21st Annual Daniel R. Biello Memorial Lecture on March 14. He spoke on “The evolution of PET/CT: a path of no return.”

Townsend (left) is shown with Barry Siegel, MD, chief of the Division of Nuclear Medicine and coordinator of the Biello Lecture.
LECTURES
Continued from page 29

Marilyn Siegel, MD, professor of radiology and of pediatrics, spoke on “Congenital bowel diseases in children” and “US/CT of acute right lower quadrant pain” at the 20th Japanese College of Radiology Mid-Winter Seminar, Fukuoka, Japan, January 18-21. She presented “CT of the pediatric chest in routine practice” and “Vascular malformations of the pediatric chest” at the 39th International Course on Diagnostic Imaging, Davos, Switzerland, March 24-30. Siegel spoke on “Sonography of acute bowel disease,” “Sonography of neonatal hydronephrosis,” and “Spinal ultrasonography” at the 16th Annual Diagnostic Ultrasound Symposium, Toledo, Ohio, March 10. She presented “Pediatric multi-slice CT angiography: How I do it” at the Society of Pediatric Radiology Annual Meeting, Miami, Florida, April 20.

Yuan-Chuan Tai, PhD, assistant professor of radiology, presented “Positron emission tomography—principles and applications” to the Department of Nuclear, Plasma, and Radiological Engineering, University of Illinois at Urbana-Champaign, February 6.

Karen Wooley, PhD, professor of chemistry and of radiology, presented “Complex, amphiphilic polymer nanostructures, originating from combinations of living polymerizations, supramolecular assembly and regioselective crosslinking” to the Department of Chemistry, Columbia University, New York, New York, February 1. She spoke on “The promise of nanotechnology in medicine” at the Frontiers in Human Pathobiology Seminar Series, Washington University in St. Louis School of Medicine, February 14. Wooley spoke on “Crafting organic nanostructures with well-defined size, shape, structure and properties” at the Chemistry-Biology Interface Seminar, University of Illinois at Urbana-Champaign, March 12. She presented “Complex constructs having nanoscale features by combining incompatible polymer components” and “Nanoparticles and nanocages originating from well-defined brush block copolymers” at the 233rd American Chemical Society National Meeting & Exposition, Chicago, Illinois, March 25-29.

Pamela Woodard, MD, associate professor of radiology, spoke on “Basic cardiac MRI” and “Delayed contrast-enhanced cardiac MRI” at the Armed Forces Institute of Pathology, Bethesda, Maryland, January 22, March 18, and April 23.

SYMPOSIA
In this section of FYI, only those faculty and staff who have Department of Radiology appointments are listed.

SOCIETY OF INTERVENTIONAL RADIOLOGISTS
32nd Annual Scientific Meeting
Seattle, Washington
March 1-6, 2007

Daniel Brown, MD, workshop coordinator, Gastrointestinal IR: Techniques and Management.

Daniel Picus, MD, panelist, Case Based Review: Non-Vascular Interventions.

Suresh Vedantham, MD, workshop coordinator, Thrombolytic Therapy of Venous Thrombolysis.

James Duncan, MD, PhD; Craig Glaiberman, MD; Benjamin Jacobs, “Expert Performance Evaluation Using Real Time Simulated Environments: data extracted from the EXPERTISE protocol.”

James Duncan, MD, PhD; Craig Glaiberman, MD, “Analysis of simulated angiographic procedures, extracting efficiency data from audio and video recordings.

Senturia Lecture

On May 2, Lane Donnelly, MD, radiologist-in-chief at Cincinnati Children’s Hospital, presented “How to perform and interpret MR cine sleep studies for obstructive sleep apnea in children” at the 13th Annual Hyman R. Senturia Lecture.

Robert McKinstry, MD, PhD, chief of pediatric radiology, presented Donnelly (right) with a commemorative plaque.

Daniel Brown, MD, PDOH, workshop coordinator, Gastrointestinal IR: Techniques and Management.

Daniel Picus, MD, panelist, Case Based Review: Non-Vascular Interventions.

Suresh Vedantham, MD, workshop coordinator, Thrombolytic Therapy of Venous Thrombolysis.

James Duncan, MD, PhD; Craig Glaiberman, MD; Benjamin Jacobs, “Expert Performance Evaluation Using Real Time Simulated Environments: data extracted from the EXPERTISE protocol.”

James Duncan, MD, PhD; Craig Glaiberman, MD, “Analysis of simulated angiographic procedures, extracting efficiency data from audio and video recordings.
Craig Glaiberman, MD; James Duncan, MD, PhD, “Measuring proficiency during renal artery stent placement using a high fidelity medical simulator.”

Ashesh Parikh, MD; James Duncan, MD, PhD; Craig Glaiberman, MD, “Recording datasets for performance assessment during medical procedures.”

Karun Sharma, MD, PhD; Jennifer Gould, MD; Daniel Brown, MD, “Survival following hepatic arterial chemoembolization (HACE) for liver dominant melanoma metastases.”

Pamela Woodard, MD, “Cardiac CT: non-coronary applications.”

SOCIETY OF BREAST IMAGING
8th Post Graduate Course Hollywood, Florida April 14-17, 2007

REFRESHER COURSE Dionne Faria, MD, MPH, “Work up of masses.”

PANEL DISCUSSION Barbara Monses, MD, “Workflow issues.”


IN-CAMERA SESSION Jay Heiken, MD, “How can we ensure high quality CT colonography?”

PRESENTATION Jay Heiken, MD, “Hepatic masses: distinguishing benign from malignant lesions.”

WORKSHOPS
Dennis Bale, MD, “ABR Update—2007.”

Jay Heiken, MD, “Imaging the pancreas: neoplastic and inflammatory disease.”

Christine Menias, MD, “CT evaluation of lower abdominal pain.”

Sharlene Teefy, MD, “Ultrasound evaluation of TIPS.”

SOCIETY FOR PEDIATRIC RADIOLOGY 50th Annual Meeting and Postgraduate Course Miami, Florida April 17-21, 2007

POSTER PRESENTATIONS
William McAlister, MD, “Deactivating germline mutations in LEMD3 cause osteopoikilosis and Buschke-Ollendorff syndrome but not melorheostosis.”

William McAlister, MD, “Hypophosphatasia: misleading in utero presentation for childhood and odonto forms.”—Award of Honorable Mention

Prakash Masand, MD; Rebecca Hulett Bowling, MD, “Multislice CT in the evaluation of unusual pediatric masses.”

CONFERENCE OF NUCLEAR CARDIOLOGY 8th International Prague, Czech Republic April 29-May 2, 2007

SCIENTIFIC PRESENTATIONS
Robert Gropler, MD, “The future of nuclear cardiology”; “Role of nuclear techniques and hybrids.”

POSTER PRESENTATION
Pilar Herrera, MS; Donna Lesniak, RN; Carmen Dence, MS; Zulfia Kirsieva-Ware, PhD, MD; Robert Gropler, MD, “Impact of hyperinsulenic-euglycemic clamp (HIEG) during cardiac work on myocardial glucose metabolism, oxidation and glycogen formation in type 1 diabetic patients.”

INTERNATIONAL SYMPOSIUM ON RADIOPHARMACEUTICAL SCIENCES 17th Annual Meeting Aachen, Germany April 30-May 4, 2007

KEYNOTE ADDRESS
Michael Welch, PhD, “Thirty years of ISRC: changes and consistencies with evolving methods and targets.”

SCIENTIFIC PRESENTATIONS
Laura Meyer; Martin Eiblmaier; Carolyn Anderson, PhD, “Potential role of tumor suppressor protein p53 in the trafficking of copper to the nuclei of tumor cells.”

Amy Vavere, PhD; Jason Lewis, PhD, “11Cu-labelling and small animal PET imaging of a Ph-dependent insertion peptide—Cu-DOTA-PHLIP.”

RADIONUCLIDE RESOURCE FOR CANCER APPLICATIONS AN NCI-SUPPORTED PROGRAM AT WASHINGTON UNIVERSITY

Jason Lewis, PhD; Lucie Tang; and Michael Welch, PhD, of Mallinckrodt Institute’s Division of Radiological Sciences, were the organizers of “Production and Application of ‘Non-Standard’ PET Nuclides”—the April 29th satellite workshop that coincided with the 17th International Symposium on Radiopharmaceutical Sciences (ISRS) in Aachen, Germany. Presenters at the workshop, which was supported by a National Cancer Institute/National Institutes of Health grant, discussed the production, use, and dissemination of the “non-standard” PET nuclides. More than 100 scientists and engineers from 20 countries attended the successful event, which will be offered again in 2009 at the 18th International ISRS.
**Symposia**

Continued from page 31

Raffaella Rossin, PhD; Michael Welch, PhD, “Small animal PET imaging of tumor vasculature using a Br-labeled human recombinant anti-ED-B fibronectin antibody fragment.”

Aviv Hagooly, PhD; Jason Paisley; Sally PhD; Robert Mach, PhD, “In vivo evaluation of imaging and drug delivery: in vivo evaluation of Cu-labeled PEG graft copolymers.”

**Poster Presentations**

Dong Zhou, PhD; Wenhu Chu; Justin Rothfuss; Lynne Jones; Chenbo Zeng; Jinhua Xu; Delphine Chen, MD; Michael Welch, PhD; Robert Mach, PhD, “Novel nanocarriers for imaging and drug delivery: synthesis of [125I]PK-11195 at WUSM.”

Gregory Gaehle; Jeffrey Willits; Stephen Moerlein, PhD; Robert Mach, PhD; Michael Welch, PhD, “Automated production of [%]fluorodopa injection, USP.”

Thaddeus Wadas; Ashley Fiamengo; Christopher Sherman; Carolyn Anderson, PhD, “In vivo evaluation of Cu-labeled cross-bridged tetraaza-macroyclic complexes with amide and/or carboxylate functional groups.”

David Reichert, PhD; Jeesong Yoo, “Cyclen-based copper complexes as potential estrogen receptor ligands: synthesis, binding affinity, and computer modeling.”

Wilson Edwards, PhD; Samuel Achilefu, PhD; Buck Rogers, PhD, “Evaluation of gene transfer using an adenoviral vector encoding somatostatin receptor subtype 2 fused to enhanced green fluorescent protein.”

Carmen Dence, MS; Jason Paisley; Sally Schwarz, RPh, MS; Stephanie Shockley; Mark Minton, MD; Robert Mach, PhD; Michael Welch, PhD, “Methodology for the routine synthesis of [3H]PK-11195 at WUSM.”

Christopher Bognar; Gregory Gaehle; Jeffrey Willits; Carmen Dence, MS; Michael Welch, PhD, “Utilizing a versatile inexpensive catalyst 3 robot to synthesize [%]fluorodihydrotestosterone (%FDHT).”

Hsiaoju Lee; Michael Welch, PhD; Robert Mach, PhD, “Developing 18F-labeled PPAR gamma antagonists for PET imaging.”

Zhude Tu, PhD; Robert Mach, PhD, “Design and synthesis of potent and selective fluorinated dopamine D3 receptor ligands.”

Stephanie Shockley; Stephen Moerlein, PhD; Michael Welch, PhD, “Evaluation of the peripheral benzodiazepine receptor as a marker of proliferation.”

Martin Eiblmaier; Richard Laforest, PhD; Buck Rogers, PhD; Carolyn Anderson, PhD, “Internalization, efflux, and dosimetry of two Cu-labeled somatostatin analogs in a human SSTR2-transfected cell line.”

Michael Welch, PhD; Jason Lewis, PhD, “Synthesis and characterization of 3,5-Ga- and 11In-CHXA ReCCMSH(ARG11) melanoma targeting peptides.”

Raffaella Rossin; Zhaohui Zhou; James Kozlowski; Michael Welch, PhD; Daniel Schuster, MD, “PET imaging of lung endothelium with Cu-labeled targeted nanoparticles.”

Amy Vavere, PhD; Jason Lewis, PhD, “Diminished CU-ATSM hypoxia selectivity and its relation to fatty acid synthase expression in prostate tumors.”

Carmen Dence, MS; Richard Laforest, PhD; Terry Sharp; Robert Mach, PhD; Michael Welch, PhD, “11C-methylated LY2181308, an antisense oligonucleotide to surviving: Part II - human dosimetry calculation.”

**American Roentgen Ray Society**

107th Annual Meeting
Orlando, Florida
May 6-11, 2007

Sanjeev Bhalla, MD, section chair, Cardiovascular Imaging.

**Presentations**

Sanjeev Bhalla, MD, “Cardiovascular imaging: acquired cardiac”; “Pulmonary embolic disease”; “Nonthromboembolic pulmonary embolism.”

Cylen Javidan-Nejad, MD, “Cardiovascular imaging: congenital.”

Christine Menias, MD, “Imaging nontraumatic abdominal pain including the pregnant patient: CT, MR or Ultrasound?”

Marilyn Siegel, MD, “Pediatric congenital heart disease: CTA/MRA and cardiac lesions”; “Neonatal neurosonography.”

Pamela Woodard, MD, “First trimester ultrasound.”

**Exhibits**

Prakash Masand, MD, “Multislice CT imaging of unusual pediatric renal masses.”
The Institute's Center for Clinical Imaging Research (CCIR), slated to open this summer, is a sophisticated bioimaging facility for basic and translational inpatient and outpatient clinical research. Investigators in the 9,000-square-foot facility, on the 10th floor of Barnes-Jewish Hospital's West Pavilion, will conduct research in computed tomography (CT), positron emission tomography (PET), magnetic resonance (MR), combined PET/CT, and ultrasound. Shown here is the April 2007 installation of a massive MR scanner.

Photograph by Mickey Wynn, MIR Photography Lab.